## ACAAI/AAAAI Joint Task Force Report

# Pearls and pitfalls of allergy diagnostic testing: report from the American College of Allergy, Asthma and Immunology/American Academy of Allergy, Asthma and Immunology Specific IgE Test Task Force

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The intended purpose of this monograph is to provide a general overview of allergy diagnostics for health care professionals who care for patients with allergic disease. For a more comprehensive review of allergy diagnostic testing, readers can refer to the Allergy Diagnostic Practice Parameters. A key message is that a positive allergy test result (skin or blood) indicates only the presence of allergen specific IgE (called sensitization). It does not necessarily mean clinical allergy (ie, allergic symptoms with exposure). It is important for this reason that the allergy evaluation be based on the patient's history and directed by a health care professional with sufficient understanding of allergy diagnostic testing to use the information obtained from his/her evaluation of the patient to determine (1) what allergy diagnostic tests to order, (2) how to interpret the allergy diagnostic test results, and (3) how to use the information obtained from the allergy evaluation to develop an appropriate therapeutic treatment plan.

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## INTRODUCTION

Physicians of all specialties commonly encounter patients with symptoms consistent with allergy. It can be difficult to determine if these symptoms are caused by an allergic mechanism (eg, perennial rhinitis caused by dust mite sensitivity vs nonallergic rhinitis with eosinophilia syndrome) or what allergen is causing the symptoms (ie, some allergens have overlapping seasons; house dust can contain multiple allergens) with the patient's history alone.

Two main categories of tests are available to assist physicians in making an allergy diagnosis: allergy skin tests and measurements of allergen specific IgE (s-IgE) antibodies from blood. In the context of the clinical history, both modalities can be of considerable help in identifying (or excluding) the particular allergens that may be causing the patients' symptoms. However, many clinicians who have not received training in allergy and immunology may not be familiar with the proper application and interpretation of these test results. The purpose of this brief monograph, designed principally for primary care health care professionals, is to provide an overview of allergy diagnostic testing. For a more comprehensive review of allergy diagnostic testing, readers are referred to the recently updated Allergy Diagnostic Practice Parameter,[1] which can also be found on the following Web sites: www.jcaai.org and www.acaai.org.

Key messages include the following:

- Allergy test results (blood or skin) should always be interpreted in the context of the patient's clinical presentation, age, relevant allergen exposures, and the performance characteristics (eg, sensitivity, specificity, reproducibility) of the allergy tests themselves.
- Allergy tests yield information on sensitization, which is not always equivalent to clinical allergy (ie, sensitivity); thus, interpretation in the context of clinical history is important. The clinical history should guide what allergens are selected for testing.
- The practical value of allergy skin or blood tests rests in their ability to give accurate and consistent results when used as a confirmatory tool.

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- Different allergy laboratory methods may not yield comparable results (eg, the level of s-IgE to milk from the ImmunoCAP is not comparable with the level measured by the Immunolite system), even if they are reported in the same units or classes.
- Variability in allergy skin testing results may be due to several factors, such as testing device, extract quality, and location of body where the testing is performed.
- Treatment decisions for allergic patients should be based on the appropriate diagnosis and the identification of causative allergens.

## IN VITRO VS IN VIVO ALLERGY TESTS

There is currently no single gold standard test for diagnosing aeroallergen (airborne) allergy. The double-blind, placebo-controlled food challenge that is considered the gold standard for food allergies is a time-consuming procedure that is limited to trained allergy specialists and carries the risk of producing a severe reaction.

The clinical history drives the diagnosis of human allergic disease. Once the history has provided a strong suggestion of IgE-mediated disease, in vivo (skin) or in vitro (laboratory) methods can be used to confirm the presence of allergen s-IgE antibody in the skin and blood, respectively. Detection of IgE antibody of a defined allergen specificity in the skin and blood simply provide confirmation of sensitization (ie, presence of allergen s-IgE positivity) not allergic disease. The clinical history makes the critical link between the allergy skin or blood test results and the allergic disease.

There are circumstances in which the allergy skin and blood tests have their distinct advantages and limitations in the diagnostic process. In general, good concordance has been identified between a positive skin test result and a positive blood test result for the most potent aeroallergens from trees, grasses, weeds, epidermal allergens (eg, cat and dog), and dust mite allergens. Variability in skin test and blood test results may be due to several factors, such as the skin test method (percutaneous vs intradermal), quality and stability of the skin testing extracts, skin test device or the laboratory assay (methods), and the biological reagents used in the laboratory assay. In general, there is good concordance between results of the allergy diagnostic tests and clinical history. Exceptions (eg, a negative skin test or serum s-IgE test result with a positive clinical history) require additional analysis or use of a different method (eg, skin testing if the serum s-IgE test result is negative). After additional analysis, if the s-IgE antibody test results (either skin test or serum s-IgE antibody analysis) remain inconsistent with the patient's clinical history, the overriding criteria in making the final diagnosis should be the clinical history and physical examination. Some studies comparing the 2 test methods have found skin tests to be more sensitive (ie, lower false-negative rate) and serum s-IgE tests to be more specific (ie, lower false-positive rate).[2,3]

## LABORATORY ALLERGY TESTS

*What Is an s-IgE Determination?*

An allergy blood test is designed to detect and measure circulating IgE antibodies, which are directed at a specific allergen, such as short ragweed. s-IgE tests were first introduced commercially in 1972. The first test evaluated IgE using radioisotopically labeled anti-IgE and was subsequently called the radioallergosorbent test (RAST). RAST, which is no longer in use, was essentially a qualitative test (ie, demonstrated whether s-IgE was present or not and did not provide quantitative information about how much s-IgE was present). Subsequent generations of s-IgE assays have been able to provide quantitative information about s-IgE. In the 1980s, more than a dozen different commercial test systems all carrying a vast number of tests for s-IgE existed in the United States. Gradually, because of market pressures and performance issues, this number began to decrease. With minor exceptions, RAST is now obsolete. However, the term *RAST* became a colloquialism for all varieties of these tests. This is unfortunate because it is well recognized that there are well-performing tests and some that do not perform so well, yet they are all called RASTs, making it difficult to distinguish which is which. For these reasons, it is now recommended that the use of RAST as a generic descriptor of these tests be abandoned.

Today, there are mainly 3 methods: Turbo RAST (Agilent Technologies Co, Santa Clara, California), Immulite (Siemens Medical Solutions Diagnostics, Tarrytown, New York), and ImmunoCAP (Phadia, Uppsala, Sweden). ImmunoCAP is the assay that has been most extensively studied. There are also some in-house developed tests available to physicians in the United States that have not been well studied or received clearance by the Food and Drug Administration (FDA). FDA clearance involves review of the performance data of both the laboratory assay and specific allergen reagent.

The basis of these tests rests on the binding of the allergen s-IgE in the patient's serum during the incubation phase of the test to allergens that have been immobilized to a solid phase (Fig 1). Extraneous materials, including nonbinding antibodies, are then eliminated by washing the solid phase, and labeled anti-IgE antibodies bind to the remaining IgE antibodies. The label may be an enzyme conjugated to the anti-IgE antibody that reacts with a fluorescent substrate. The measured fluorescence from the enzyme-substrate reaction conjugated to the anti-IgE antibody is proportional to the amount of allergen s-IgE bound in the serum sample. This is calculated by interpolation from a standard calibration curve. The total calibration curve used in most test systems today is linked to the World Health Organization IgE standard and reported in arbitrary mass units (kilo international units of allergen specific antibody per unit volume of sample [kUa/L]).

Some s-IgE assays report results in a class system (class I-VI) based on the amount of detected s-IgE. However, the class system has become obsolete with the quantitative reporting of s-IgE using kUa/L.

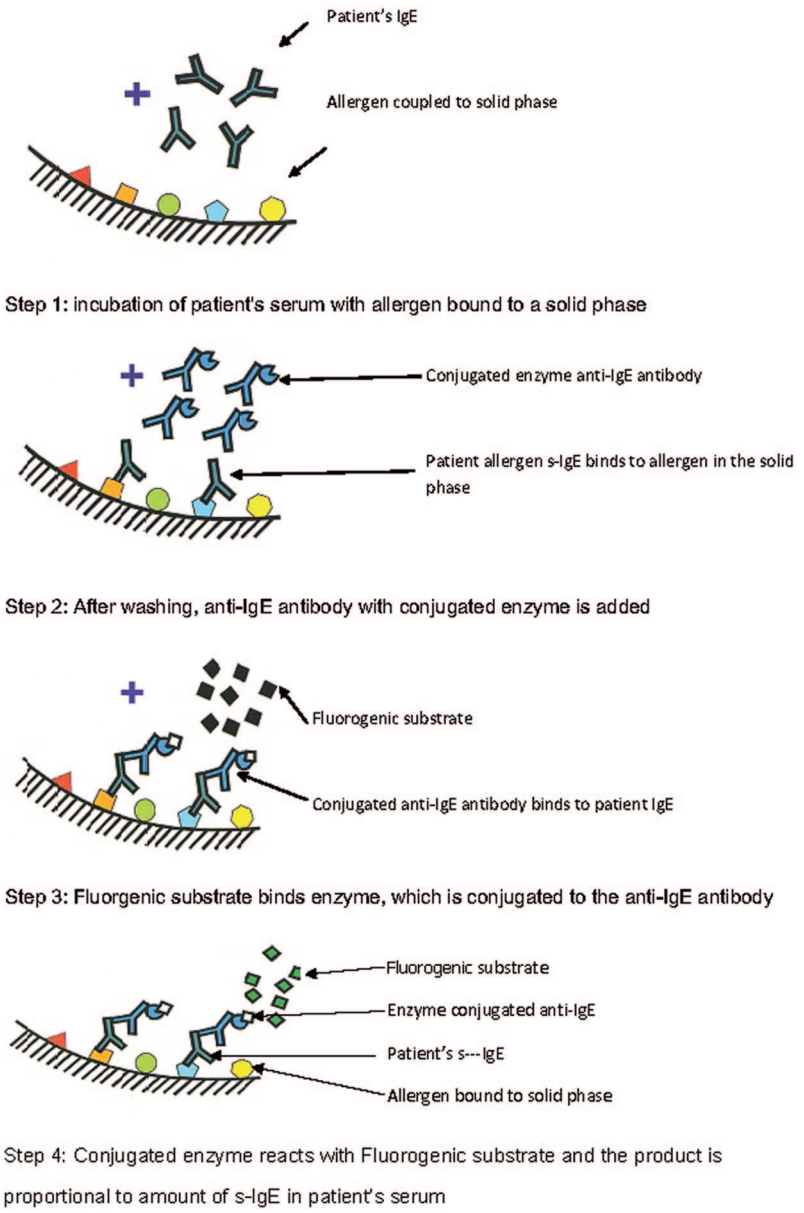


Figure 1. Binding of the allergen specific IgE (s-IgE) in the patient's serum during the incubation phase of the test to allergens that have been immobilized to a solid phase. Provided and modified with permission by Jay Portnoy, MD.

In the ImmunoCAP system, 1 international unit is equal to 2.42 ng of s-IgE.[4,5] The conversion ratios have not been established with other systems. Results from different s-IgE systems (eg, Immulite, ImmunoCAP, Turbo RAST) are not always comparable to each other even if they are provided in the same units.[4]

*What Allergens Should Be Tested?*

Since there are numerous allergens in every patient's environment, clues from the patient's history and known exposures are essential in narrowing down specific tests to order. Often this is obvious when a patient's complaints can be associated with specific exposures, such as a pet or a particular pollen season. Because most allergic patients are sensitized to multiple allergens,[6] the task of determining which ones are of major importance is not a simple task. The level of s-IgE or skin test size (see the skin test section) to a given allergen can be helpful, with higher levels being more likely to be associated with clinical allergy. Because exposure to multiple allergens to which a patient is sensitized is likely to create a synergistic effect, optimal management may require

identification and management for each of the relevant allergens. Panels of tests designed for specific seasons and geographical locations are available for this purpose.

*How to Interpret Allergy Laboratory Test Results*

Allergy tests demonstrate whether the patient has s-IgE or not (ie, sensitization) but do not determine if the s-IgE is the cause of their symptoms (ie, allergic). Therefore, the selection of allergens for testing should not be ordered randomly but instead be based on symptoms, environmental and occupational exposures, age, and other relevant factors (eg, hobbies), and all allergy test results need to be interpreted in the context of the clinical history.

Allergen sensitization and exposure to the sensitizing allergen have been associated with reduced lung function and the persistence of wheeze in children.[7–9] The level of s-IgE to a given allergen(s) is an important consideration because it has been demonstrated with several different inhalants and foods that the probability of symptoms will increase with increasing amounts of s-IgE.[10–12] Concomitant viral infections have been shown to be an important consideration in the exacerbation of allergic symptoms.[13] The level of s-IgE is predictive of risk for hospitalization in asthmatic patients with viral infections.[14] In adults, the level of s-IgE to various inhalants is predictive of chronic rhinitis and asthma severity.[15] The degree of skin test reactivity and level of venom s-IgE correlate with the frequency, but not severity, of systemic reactions to insect stings.[16] The level of s-IgE may predict who will have a positive food challenge result.[17] Thus, knowing the quantity of the s-IgE may be important in patient evaluation.

*Sensitization vs Clinical Allergy*

For example, if a patient had been exposed and sensitized in Saudi Arabia to a camel but is not exposed to camels in North America, the presence of these antibodies is not likely to be related to symptoms unless the individual recently visited a zoo. In this case, the patient may be clinically allergic to camel, but without exposure this allergen would essentially be irrelevant and not the cause of their current allergy symptoms. Patients can also have s-IgE to substances that produce no symptoms with exposure. For example, a child may have s-IgE to milk but drinks daily with no adverse effects. In this case, the patient is sensitized but not clinically allergic to milk.

*Test Performance Issues*

In the United States, several different test formats are available for determining s-IgE. Some of these have been extensively studied, whereas others have not. Recent publications have confirmed that the results of one test are not generally comparable to those of another.[4,18] Thus, physicians ordering these tests should be aware of the assay their laboratory is using. The difference in the performance patterns of different laboratory tests was demonstrated in a study that compared the 3 commonly used systems in the United States: Turbo RAST, Immulite, and ImmunoCAP.[4] The study found poor agreement in the qualitative testing (ie, detecting presence of s-IgE [sensitization]) among the 3 assay systems, with the Turbo RAST being the most variable. Significant discrepancies were also found with the quantitative evaluations (amount of s-IgE) with "Immulite overestimating and Turbo RAST underestimating s-IgE compared with ImmunoCAP."

One blinded study that sent 12,708 samples to 6 major laboratories in the United States that used 5 different assays found that the 1 laboratory assay (ImmunoCAP) used by 2 laboratories "performed nearly as well as the ideal standard, with an overall average slope (0.97; range, 0.91 to 1.01), SE (0.05; range, 0.02 to 0.16), and … coefficient of variation (10.3%; range, 6% to 14%)."[18] "Extensive variability was observed in the other 4 laboratory-assay systems with respect to overall average slope (0.76; range, 0.11 to 1.24), and percent with a coefficient of variation (19%; range, 5% to 49%). For some specific allergens, some laboratories' assays were not able to detect serial dilutions of the same sample." The authors concluded these 4 laboratory assays had a "substandard overall performance with multiple instances of poor precision and accuracy, particularly for certain allergens, such as weeds and molds." These studies suggest various assays measure different populations of IgE antibody. Currently, it is not known which of the major assays provides the most accurate evaluation of allergen s-IgE in patients' serum.

*Laboratory Considerations*

The quality of the allergy diagnostic test influences the physician's diagnosis and treatment. With respect to the diagnostic allergy laboratories, a number of measures are taken to ensure good results. These measures include FDA clearance of the test procedure used, laboratory licensing and accompanying inspections by public health officials, and periodic proficiency testing on blinded specimens. These measures and recommendations for manufacturers, laboratories, and users have recently been elaborated in the Clinical Laboratory Standards Institute's guidelines for immunological assays of IgE and s-IgE. Physicians should be aware of which laboratory assay method was used (eg, ImmunoCAP, Immulite, Turbo RAST), whether or not the laboratory is licensed by the Clinical Laboratory Improvement Amendments, and its performance on proficiency testing during the past year. These measures go a long way to ensure that laboratory tests are performed by trained individuals and the results are reliable.

*Summary of Allergy Laboratory Testing*

Measurements of s-IgE have continued to become more reliable and better defined. In the future, we can anticipate that tests will provide quicker results and the relationship between the test results and clinical allergy (ie, degree and magnitude of symptoms) will be better understood. Laboratory allergy tests will probably not become the single diagnostic test for clinical allergy but are likely to be an important objective means of confirming clinical impressions based on the clinical history. Potential performance variability among the different allergy-laboratory assays means the results of the different assays are not interchangeable and underscores the importance of knowing what laboratory assay was used when evaluating the test results.

## ALLERGY SKIN TESTING

Skin tests for allergic disorders were first described in 1867 and quickly evolved into the scratch test, which was initially used to confirm the diagnosis of food allergy in children. In clinical practice, the scratch has given rise to the prick or puncture test, and in some cases if the results are interpreted as negative, it is followed by the intradermal test.

In the allergist's office, skin testing remains the primary test to confirm an allergic response for several reasons. Skin testing is minimally invasive and when performed correctly has good reproducibility. It is also preferred because the tests results are available within 15 minutes of the test application, which will assist the allergist in developing an appropriate treatment plan on the initial consultation. Skin testing is easily quantifiable and can allow the evaluation of multiple allergens in 1 session. In general, there is a good correlation with the results of in vivo challenges (eg, conjunctival, nasal, or bronchial allergen challenges), although both false-positive and false-negative results may occasionally occur. Both methods of allergy diagnostic testing, in vitro (serum s-IgE) and in vivo (skin tests), may be relied on in the evaluation of allergic rhinitis, asthma, food allergy, insect sting allergy IgE-mediated anaphylaxis, and certain occupational allergic diseases. Skin testing may also be helpful in the diagnosis of allergic reactions to drugs (especially in the evaluation of $\beta$-lactam and allergy to anesthetic agents). Skin testing may be impracticable in severe eczema or in patients who cannot discontinue the use of medications that have antihistaminic effects, such as histamine$_1$-antagonists and tricyclic antidepressants. In these cases, measurement of serum s-IgE may be more appropriate.

*Variables That Affect Skin Test Results*

When considering skin testing, it is important that the technician performing the skin tests and the clinician ordering or interpreting the results of these tests be aware of factors that may influence or confound the results. These factors include type of skin testing, device used, placement of tests (location and adjacent testing), the quality of the extracts used, and the potential confounding effects of medication. As for any diagnostic test, it is important that the clinician consider the positive and negative predictive value of the tests being performed.

Certain medications may affect the response and alter the validity of the prick or puncture and intradermal tests. These include first- and second-generation antihistamines and some tricyclic antidepressants. Leukotriene antagonists do not appear to have a significant effect. Patients currently receiving $\beta$-adrenergic blocking agents and monoamine oxidase inhibitors may have problems in responding to epinephrine if a reaction should occur while the patient is undergoing skin testing. Although adverse reactions to skin prick testing are rare, a cautious attitude should be adopted when considering allergy testing in patients who are taking $\beta$-adrenergic blocking agents.

In the diagnosis of suspected IgE-mediated allergic diseases, neither skin tests nor in vitro IgE tests should be either requested or interpreted outside the context of the clinical history and physical examination. Positive test results provide objective confirmation of IgE sensitivity, which may support a history of symptoms on exposure to the relevant allergen. In contrast, a negative test result makes allergy to a suspected allergen less likely. When used indiscriminately, both skin and in vitro IgE tests may commonly be associated with false-positive results and, rarely, false-negative results may occur. Thus, diagnostic tests should be used to support or exclude a diagnosis of specific allergies based on the history. As with in vitro testing, skin tests should almost never be used as a substitute for a careful history or as an allergy screen.

*Variables That May Affect Skin Test Reactivity*

The following variables may affect skin test reactivity:

- age (reactivity decreases with age; actually peaks in the late teens to early 20s and then decreases over time)
- histamine sensitivity (inherent inborn sensitivity may increase or decrease skin test reactivity)
- location on the body (which location [upper vs. lower back and back vs arm] may vary with device)
- chronobiology (circadian and circannual variability)
- other diseases (cancer may suppress skin test reactivity)
- sun damage of skin (affects mast cell number and may explain at least some of the loss of skin test reactivity with aging along with decrease in IgE with age)
- allergen immunotherapy (effective immunotherapy decreases skin test reaction to the treated allergen)
- allergen extract quality (weaker extracts may produce false-negative results)
- proximity to the positive control or other allergens (bystander effect —if an allergen extract is placed too close to a strong positive extract this may produce a false-positive result)
- medications (some can increase, eg, $\beta$-blockers, and other can decrease skin test reactivity, eg, antihistamines and tricyclic antidepressants)

*Methods Used for Allergy Skin Testing*

Skin testing may be performed using either prick or puncture (percutaneous) or intradermal (intracutaneous) techniques. Intradermal testing is more sensitive than prick or puncture testing,[3] and as a result, the extract for prick or puncture testing must be at least 1,000-fold more concentrated to achieve a similar level of sensitivity. Although intradermal may be more reproducible than prick or puncture testing, there are many factors that favor the routine use of the prick or puncture test for allergy testing. These factors include economy of time, patient comfort, and safety.[19]

*Prick or puncture (percutaneous) method.* Prick or puncture tests are performed with either a single or multitest device. A consistent amount of allergen is placed on a device that punctures the skin approximately 1 mm at a 90° angle. It is important to adequately train the technician applying the skin test to achieve consistency in each individual site. A positive control (histamine) and a negative control (saline or 50% glycerinated human serum albumin-saline) should be applied at the same time as the allergens. Multiple double-

blind, placebo-controlled studies have shown the clinical usefulness of the prick or puncture test, with sensitivities as high as 90%. This has been shown in outdoor park studies and indoor studies where the environment is controlled. The prick or puncture test is an extremely reliable diagnostic test for several foods, including milk, eggs, and peanuts, especially in those with the more severe symptoms.

Prick or puncture tests may be performed in infants as young as 1 month. The sensitivity remains relatively stable through the fifth decade and is still valid well beyond the age of 65 years.[20] There may be variation in wheal size related to the area of the test where the test is placed, and skin tests should not be performed on areas with dermatitis or severe dermatographism.

The safety of skin prick or puncture tests is well established.[21] Analysis of fatal reactions from 1990 to 2001 showed no instances of near-fatal or life-threatening reactions to inhalant prick or puncture tests.[22] Only 1 fatal reaction occurred in a patient with moderate persistent asthma after application of 90 good food prick tests.

*Intradermal (intracutaneous) method.* Intradermal tests are used by clinicians when prick or puncture test results are negative but the history appears convincing of allergy. This procedure is more sensitive but less specific than the prick or puncture method.[2] Some studies have demonstrated that a positive intradermal test result with a negative skin prick test result correlates poorly with clinical sensitivity.[2,23] Intradermal tests are commonly used in the diagnosis of stinging insect (eg, wasp, yellow jacket) and drug allergies. Drug classes that have been associated with IgE-mediated (ie, allergic) reactions include cancer chemotherapeutic agents, muscle relaxants, insulin, and heparin.

### *Adverse Reactions to Allergy Skin Tests*

Immediate systemic reactions are more common with intradermal tests than prick or puncture skin tests. Six fatalities have been reported previously by the American Academy of Allergy, Asthma and Immunology, 5 of which were in asthma patients who were not prescreened with the prick or puncture tests.[24] There was 1 fatality reported in the 11-year survey of fatal reactions mentioned previously.[25] In a study of 16,205 Americans that investigated a variety of routine medical procedures, including prick or puncture tests and venipuncture, there was a significantly greater incidence of adverse reactions with venipuncture than prick or puncture tests (adverse reaction rates for venipuncture, 0.49%; 95% confidence interval, 0.38%–0.60%; adverse reactions for prick or puncture tests, 0.04%; 95% confidence interval, 0.01%–0.08%.[26] There were no episodes of anaphylaxis and 1 episode of asthma during venipuncture. The remainder of the reactions were syncope, near syncope, and malaise.

### *Types of Devices Used for Allergy Skin Testing*

Although intradermal tests are only performed using a hypodermic syringe and needle, prick or puncture tests may be performed with a variety of devices. Although some devices have a single stylus with a single or several points, others have multiple heads and allow up to ten tests to be accomplished with 1 application (Fig 2). These testing devices vary in the degree of trauma that they inflict on the skin. Thus, the size of positive responses and also the likelihood of producing a false-positive result at the site of the negative control or allergen test sites control test that produced a negative response may differ among different devices.[27–29] Interpreting the results of the allergen tests with the positive and negative control will help account for the skin test variability due to the testing device; an inadequate or absent positive control would suggest there may be false-negative reactions, which can be due to histamine-blocking medications or other factors that may interfere with skin test reactivity and a positive negative control may suggest false-positives reactions, which can be due to device trauma or dermatographism.

### *Ways of Reporting Allergy Skin Test Results*

The skin test report should include the measurement of the positive and negative control, and the reactions to the different allergens tested should be interpreted in light of the size of the positive and negative controls. For example, if the positive control has no reaction, then nonreacting allergen test results cannot be considered negative because of the possibility of some factor interfering with the skin test response, such as an antihistamine, leading to a false-negative results. Likewise, if the negative control has a positive reaction due to device trauma or dermatographism, the size of the negative control needs to be considered when interpreting the positive allergen test results. In many studies, a positive skin test result is considered a wheal that is 3 mm or greater than

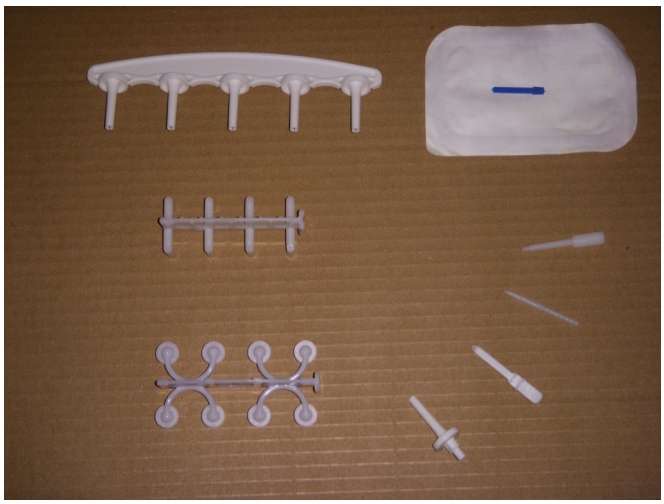

Figure 2. Examples of different skin test devices (multiheaded and single). Photography by Michelle Schwartz, provided with permission by Linda Cox, MD. Left side (multitest devices) from top to bottom: Quintest multiple skin test device by Hollister-Stier; ulti-Test II multiple skin test applicator by Lincoln Diagnostics; ick-Test Applicator by Panatrex, Inc. Right side skin testing devices (single test devices) from top to bottom: AllerSharp by Quorum allergy products; GreerPick by Greer Labs; Duotip-Test by Lincoln Diagnostics, Inc; Accu-Set by Alk-Abello, Inc; Quintip by Hollister Stier.

the negative control with 10 mm or more of surrounding erythema or flare. Skin test results are often reported in semiquantitative terms as only positive or negative or on a scale of 0 to 4 or more without indication of what size these numbers represent. For numerous reasons, allergy patients may have to change their physician. Thus, it is important that prior allergy testing records be interpretable by the receiving physician, which may avoid the need for subsequent skin testing. Reporting the skin test result as the longest diameter of the wheal and the surrounding erythema or flare is a more precise way of reporting skin test results, and this method correlated well with a computerized measurement of the actual area of the skin test reaction.[30]

Standardized allergy skin test forms are on the American Academy of Allergy, Asthma and Immunology Web site (www.aaaai.org; see the Appendix for an example of a completed skin test form). The recommended method for reporting allergy skin test results in this standardized form is the longest diameter in millimeters of the wheal and corresponding erythema or flare (see Figs 3–6 for examples of percutaneous skin test results).

*Quality Assurance Measures That Skin Testing Should Undertake: Allergy Technician Proficiency Testing*

For all allergy skin tests and s-IgE tests, quality assurance standards should be used and met. All technicians who perform skin testing should undergo an evaluation. The Clinical Laboratory Standards Institute recommends such quality control procedures for daily performance of s-IgE testing, with a recommended coefficient of variation of less than or equal to 15%. The recent Childhood Asthma Management Program study required a coefficient of variation of less than 30% be attained to confirm proficiency in skin testing.[31]

*Allergy Skin Test Quality Assurance*

Like all other laboratory tests, skin test quality assurance standards should be met to ensure that accurate testing technique is being performed. To confirm such standards, it is recommended that all technicians performing skin testing undergo evaluation of their technique. Suggested proficiency testing is 10 alternating positive (histamine) with 10 negative (saline) controls. For the histamine control, calculate the mean and SDs of each mean wheal diameter and determine the coefficient of variation (CV), which represents reproducibility (CV = SD/mean wheal diameter × 100). The quality standard should be less than 30%. For the saline control, all negative controls should be less than 3-mm wheals and less than 10-mm flares.

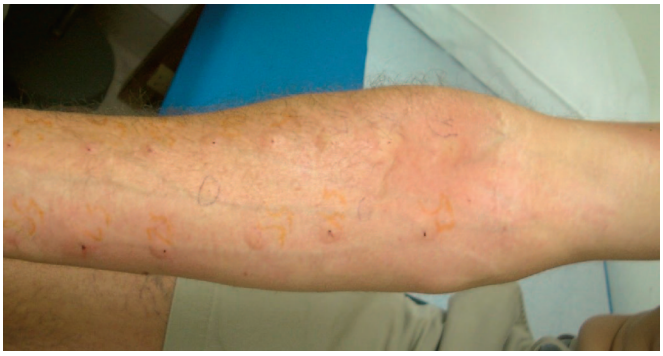

Figure 3. Percutaneous allergy skin test results: measuring the wheal and flare and erythema. Provided with permission by Linda Cox, MD.

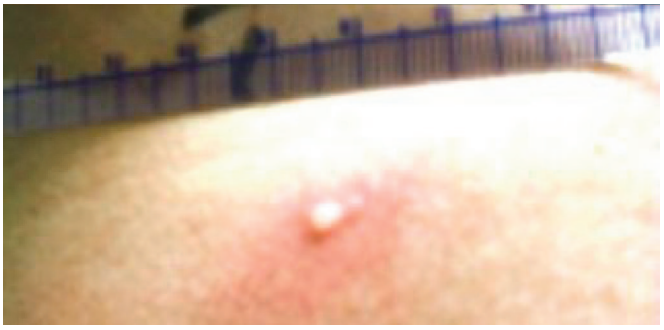

Figure 4. Percutaneous allergy skin test results: measuring the wheal and flare and erythema. Provided with permission by Linda Cox, MD.

## CONCLUSION

*Summary of Allergy Skin Testing*

Skin testing remains an invaluable tool in the diagnostic evaluation of the allergic patient. The prick or puncture test is generally the preferred method for several reasons, including patient comfort and time, cost, and safety. As with in vitro allergy tests, a number of variables affect results, such as the skin test device or the location where the tests are performed, and these variables should be noted in the skin test report. The skin test report should also include a positive and negative control. The recommended method for reporting the skin test results according to a standardized form is the measurement in millimeters of the longest diameter and corresponding erythema or flare.

*Role of Allergy Diagnostic Testing in the Evaluation of Food Allergy*

A food allergy is typically defined as an adverse immune response to the proteins in a food. This may occur as the result of a humoral response (IgE antibody), a cellular response (eg, T cells), or both. This monograph does not present a comprehensive approach to the diagnosis and management of adverse reactions to foods; rather, it summarizes the appropriate focus of an initial primary care office–based evaluation with emphasis on using serum s-IgE tests. For more comprehensive reviews of food allergy testing, the readers are referred to the Food Allergy Practice Parameter[32] or the American Academy of Allergy, Asthma and Immunology practice paper on food allergy diagnosis.[33] Although approximately 20% of people alter their diet for perceived adverse reactions to foods, it is estimated that only 3% to 5% have an immune response (allergy). Unnecessary food avoidance could have social, emotional, and nutritional conse-

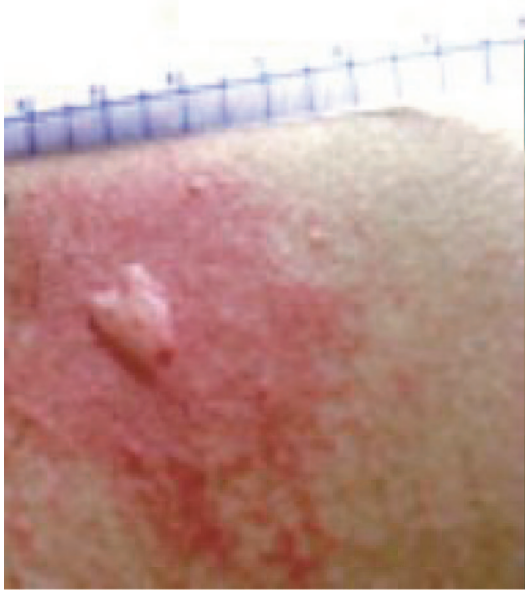

Figure 5. Percutaneous allergy skin test results: measuring the wheal and flare and erythema. Provided with permission by Linda Cox, MD.

quences, so addressing concerns about food allergy or intolerance is crucial. Similarly, foods can cause life-threatening anaphylaxis, so identification of a trigger or triggers is necessary to ensure that the proper target for avoidance is identified. Immediate (typically within minutes to an hour) allergic reactions with classical IgE-mediated symptoms, such as urticaria, wheezing, or cardiovascular symptoms, are expected to be associated with detectable IgE antibodies to the trigger food proteins. Some chronic inflammatory disorders are also associated with detectable food s-IgE antibodies. These disorders include eosinophilic gastroenteropathies and moderate to severe atopic dermatitis in children. There is not always a perfect correlation of positive allergy test results with causal food proteins. Specifically, a test result may be positive to a food that does not induce a reaction (ie, sensitization but not clinically allergic) or may be negative to foods that cause an inflammatory response through a non–IgE-mediated immune mechanism. There are well-recognized allergic gastrointestinal disorders, such as food-induced enterocolitis syndrome (severe vomiting in an infant, often leading to dehydration and failure to thrive), that are mediated by T cells, and test results for food s-IgE are typically negative.[34,35] Certain chronic allergic inflammatory disorders are not typically related to a food allergy but more often to environmental allergies (ie, allergic rhinitis, asthma). Food allergy is also not typically related to symptoms of headache, hyperactivity, fatigue, or pain. IgG and IgG4 antibodies to food antigens are not useful in assessing food allergy.[36]

The history is a primary modality to determine if further diagnostic testing and/or referral to an allergist is needed. Important components of the history include relationship of symptoms to ingestion of a potential trigger, the timing of symptoms, and the symptoms themselves. The history may identify a nonallergic cause for symptoms (intolerance, pharmacologic effect), may exclude or implicate IgE antibody–associated mechanisms, and may help to identify specific causal foods. Testing should not proceed if symptoms are not likely to be food related or not likely to be associated with IgE. A convincing history (for example, 2 episodes of anaphylaxis to isolated ingestion of walnut) with a positive test result (in this example for walnut s-IgE) provides excellent diagnostic accuracy. In some situations, the history and/or test results may be indeterminate, in which case an allergist may use more sensitive tests (skin tests, elimination diets, and physician-supervised oral food challenges) to confirm or refute a specific food trigger.

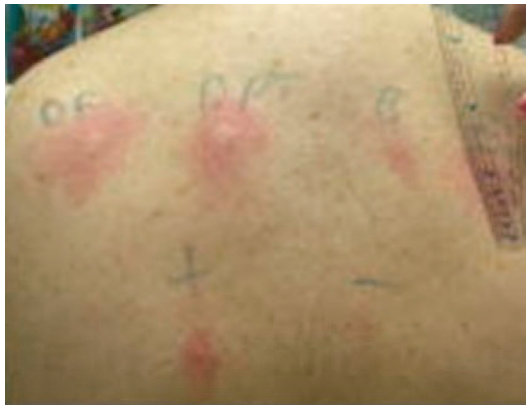

Figure 6. Percutaneous allergy skin test results: measuring the wheal and flare and erythema. Provided with permission by Linda Cox, MD.

Several manufacturers have in vitro assays to measure food s-IgE antibodies. Advantages of testing for food s-IgE antibodies using serum intrinsically include availability in a primary care office setting and good sensitivity (approximately 70% to 90%) and specificity (approximately 50% to 80%). Another modality to identify food s-IgE is a skin prick test with commercial extracts or, in some cases, fresh extracts of the suspected food. The skin tests are primarily available to the allergist. In some cases, the skin test may be more sensitive than the serum tests,[2,37–39] and additional advantages compared with blood tests include lower cost and immediate results. However, the in vitro tests can be used in some situations where skin tests cannot, for example, if a patient has an extensive rash or is using antihistamines.

The tests are sensitive, but they disclose the presence of food s-IgE (sensitization). This does not always correlate with true clinical reactions when the food is ingested (clinical allergy).

It must be appreciated that certain food-responsive disorders are rarely (food protein–induced enterocolitis syndrome) or only sometimes (eosinophilic esophagitis) associated with detectable food s-IgE antibodies. Therefore, a negative test result does not rule out food sensitivity in these disorders.

It is typically stated that more than 85% of significant food allergy is attributable to egg, milk, peanut, wheat, soy, tree nuts (eg, walnut, cashew), fish, and shellfish. Seeds seem to be emerging allergens (eg, sesame).[40] However, any food can

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**Hollywood, Fl. 33424**
**Telephone: 645-123-4444 Fax: 645-123-4567**

**Patient name**: **Jerry Cleanex** **Date of birth: 05/05/90** **Patient number**: **23456**
**Testing Technician**: Mary Lancet
**Last use of antihistamine (or other med affecting response to histamine)**: **10** days ago medication _____
**Testing Date (s) and Time**: **Percutaneous 5/30/02__10:30_AM Intradermal** 6/2/02 11:15 **AM**

***General information about skin test protocol***

1. **Percutaneous** reported as: **Allergen: Testing concentration: Extract compan**y (*see below)
   **Location**: back_X__arm___ **Device**: HS Quintip_____
2. **Intradermal**: 0.02ml injected, **Location**: arm **Testing concentration**: 1:500 w/v, 100 BAU or AU/ml, 400 PNU
3. **Results** Longest diameter *(Left in this example)* **or** longest diameter and orthogonal diameter (*Right in this example*) of wheal (W) and erythema (flare) (F) measured in millimeters at 15 minutes

**Blank in results column indicates test was not performed, O=negative**

* Extract manufacturer abbreviations: G=Greer, AL= Allergy Labs (Oklahoma), AK=ALK Abello, AD=ALK (Denmark), H=Hollister–Stier, AG=Antigen, N=Nelco, AM=Allermed,, AT=Antigen

| **Allergen: Concentration: Extract Manufacturer. *** | **Percutaneous W (mm) F** | | **Intradermal W (mm) F** | | **Allergen: Concentration: Extract Manufacturer. *** | **Percutaneous W (mm) F** | | **Intradermal W (mm) F** | |
|---|---|---|---|---|---|---|---|---|---|
| **Trees** | | | | | **Weeds** | | | | |
| ***Ulmaceae*** | | | | | ***Composite family*** | | | | |
| 1. American Elm 1:20 G | **0** | **0** | | | 21. Mugwort 10,000 PNU AD | **4/6** | **18/15** | | |
| ***Cupressaceae*** | | | | | 22. Short Ragweed 1:10 H | **10/6** | **20/20** | | |
| 2. Mountain Cedar 1:10 AL | **0** | **0** | | | ***Chenopod*** | | | | |
| ***Betulacea*e** | | | | | 23. Russian Thistle 1:20 AG | **3/7** | **10/15** | | |
| 3. Paper Birch 1:20 AK | **3** | **15** | | | 24. Burning Bush 20,000 PNU N | **4/6** | **15/20** | | |
| 4. Red Alder 1:20 AD | **3** | **10** | | | 25. Lamb's Quarter 1:40 AM | **6/10** | **15/20** | | |
| ***Fagaceae*** | | | | | ***Amaranth*** | | | | |
| 5. White Oak 1:10 H | **0** | **0** | **10** | **20** | 26. Red Root Pigweed G | **8/10** | **20/30** | | |
| 6. Red Oak 1:10 AG | **5** | **15** | | | ***Plantaginaceae*** | | | | |
| ***Aceraceae*** | | | | | 27. English Plantain AK | **10/9** | **20/18** | | |
| 7. Box Elder 1:20 N | **0** | **0** | | | **Molds/Fungi** | | | | |
| ***Oleaceae*** | | | | | 28. Alternaria alternata AD | **10/9** | **20/18** | | |
| 8. White Ash 1:20 AM | **0** | **0** | | | 29. Cladosporium herbarum H | **0** | **0** | **15/18** | **25/20** |
| 9. Olive 1:20 G | **5** | **20** | | | 30. Cladosporium cladosporioides AG | **0** | **0** | **18/22** | **30/35** |
| ***Salicaciae*** | | | | | 31. Penicillium chrysogenum N | **4/5** | **15/10** | | |
| 10. Cottonwood Eastern 1:40 AL | **6** | **25** | | | 32. Aspergillus fumigatus AM | **5/7** | **20/16** | | |
| ***Moraceae*** | | | | | 33. Epicoccum nigrum G | **0** | **0** | | |
| 11. Mulberry 1:20 AK | **7** | **30** | | | 34. Helminthosporium solani AL | **0** | **0** | | |
| ***Juglandacea*e** | | | | | | | | | |
| 12. Pecan 1:20 AD | **0** | **0** | | | **Animals/Mites /Cockroach/Others** | | | | |
| 13. Black Walnut 1:20 H | **0** | **0** | | | 35. D. Pteronyssinus AK | **20/30** | **40/30** | | |
| ***Plantaceae*** | | | | | 36. D. Farinae AD | **15/9** | **32/40** | | |
| 14. Sycamore 1:40 AG | **0** | **0** | | | 37. American Cockroach H | **5/6** | **12/10** | | |
| | | | | | 38. German Cockroach AG | **7** | **18** | | |
| **Grasses** | | | | | 39. Cat Epithelium N | **15** | **30** | | |
| 15. Bahia 1:20 N | **20** | **40** | | | 40. Dog Epithelium 1:20 AM | **0** | **0** | **15** | **25** |
| 16. Bermuda 10,000 BAU/ml AM | **15** | **35** | | | **Controls** | | | | |
| 17. Sweet Vernal 1:20 G | **25** | **40** | | | **Percutaneous** | | | | |
| 18. Timothy 100,000BAU/ml AL | **30** | **45** | | | **Negative:** 50% glycerine-saline G | **0** | **0** | | |
| 19. Johnson 1:10 AK | **15** | **30** | | | **Positive:** Histamine 1mg/ml AL | **5/7** | **20/15** | | |
| **Weeds** | | | | | **Intradermal** | | | | |
| ***Polygonaceae*** | | | | | **Negative**: 0.05 % glycerine-saline AK | | | **0** | **7/8** |
| 20. Sheep sorrel H | **4/9** | **15/12** | | | **Positive:** Histamine 1mg/ml AD | | | **15/20** | **25/15** |

**Interpretation:**

Appendix 1. An example of a completed allergy skin test from http://www.aaaai.org/members/only/.

potentially trigger an allergic response. Test selection is crucial because persons with atopic disease are often sensitized to numerous allergens that they tolerate when the food is ingested. A general outline of consideration in identifying foods that may be triggers and worth testing or are unlikely and not worth testing follows:

- Foods tolerated should not be tested.
- Foods not often ingested are more likely triggers if a mixture of foods resulted in symptoms.
- Foods commonly associated with severe reactions include peanut, nuts from trees, fish, shellfish, seeds, and milk.
- Common allergens for children with moderate-severe atopic dermatitis include egg, milk, wheat, and soy.

Allergy testing is generally not advised when a disorder is not associated with food s-IgE. For example, testing would be reasonable if a patient experienced typical allergic symptoms, such as urticaria or anaphylaxis, soon after ingestion of a potential food trigger. IgE tests for food would not be appro-

priate to diagnose disorders such as celiac disease, nonspecific complaints (headache), or symptom complexes likely associated with non–IgE-mediated food allergy, such as lactose intolerance. There are no IgE tests for food additives. These reactions are uncommon and not typically associated with IgE. Once it is decided to test, selection of food(s) to test requires a careful history and an understanding of epidemiologically common food allergens so that testing is directed to likely candidates. Tests for IgE to specific foods have modest sensitivity and specificity, so prior probability (based on the history) is crucial in test selection and interpretation.

*Interpretation of Serum Food s-IgE Results*

The higher the concentration of food s-IgE antibodies, the more likely there will be a clinical response to the food ingested.[12,17,41–45] Some studies (which so far have addressed only certain assay systems, a few foods, and limited age groups and disorders) show that at particularly high IgE values the chance of clinical reactions is almost certain.[17] However, the exact "diagnostic level" has varied somewhat among studies. Age, disease, and possibly other subtle nuances account for differing results among studies thus far. Caution is needed in test interpretation. In several studies that involve several foods, persons with "undetectable" levels of food s-IgE have had reactions on oral food challenge.[17,40,43,45,46] This observation demonstrates the importance of interpreting the test results in the context of the clinical history and to consider additional evaluations (eg, allergy skin prick tests, physician-supervised oral food challenges) when suspicion of allergy is high but serum test results are undetectable.

In addition, there are potential pitfalls in interpreting s-IgE test results. For example, cross-reactivity among food groups and pollen can result in clinically irrelevant positive test results to related proteins in foods. For example, food allergy is a rare cause of chronic asthma or rhinitis, whereas pollen allergy may result in positive test results to foods; testing for foods in these "wrong" circumstances may be positive to ones such as peanut or wheat that contain proteins also found in grass or birch pollens yet do not contribute to disease (in regard to the foods).

*Helpful Points to Consider in Food IgE Testing*

There are many serum tests offered, but rational selection and understanding of limitations are required to effectively select and interpret the tests. Here are additional helpful hints:

- Egg white is the major egg allergen. Typically, there is no need to test yolk or whole egg.
- Cow milk is a good test for cow's milk allergy. Typically, there is no advantage to test milk proteins ($\alpha$-lactalbumin) or foods that have milk (eg, cheese).
- There are no verified reliable IgE tests for additives or colors. Reactions to these are rare and not typically mediated by IgE.
- Clinical cross-reactivity rates are often lower than test results would indicate (eg, a peanut allergic individual often [>50%] has positive test results to multiple legumes, but reaction rates to these other legumes are approximately 5%).
- Persons with pollen allergies may test positive to numerous fruits or vegetables that may induce no or mild (oral) symptoms but only rarely severe reactions.
- Persons with atopic dermatitis may test positive to many allergens, but many are tolerated (based on supervised food challenges).
- Although chocolate, citrus, berries, and corn are often listed in allergen panels, they are uncommon food allergens.
- Food s-IgE concentrations may decline as an allergy is "outgrown."
- Clinicians must be aware that a test result may be reported in units such as classes, counts, percentage, or kUa/L, which are not comparable with each other.
- When comparing food allergy tests performed with different laboratory assays, it is important to recognize that different test methods and procedures, even when reporting the same units (eg, kUa/L), may not be comparable.

In summary, it is important to select tests and interpret results in the context of the medical history. Ordering panels of tests for foods is not recommended.

*A Word About Treatment*

The primary treatment of a food allergy is to avoid the trigger food. Accurate identification of a trigger food is crucial for patient safety. Unnecessary avoidance carries risks (eg, nutritional, social). Once a food allergen is identified, education is needed to ensure avoidance. Such education includes information about label reading, restaurant meals, cross-contact in food preparation, and many other factors. For those with life-threatening food allergies, an action plan must be in place to promptly treat reactions (eg, self-injectable epinephrine). Patients must be instructed on how to use the device, when to use it, and when to seek additional care. Consultation with an allergist is indicated to confirm allergies (which may require skin tests and oral food challenges), address avoidance and treatment, and monitor for tolerance.

Sometimes tests can be misleading if they are performed without considering intrinsic test limitations and important points from the history. For example, a 37-year-old man with allergic rhinitis has anaphylaxis from an almond cookie purchased in a bakery. A "nut panel" is ordered with the following results: cashew, less than 0.35 kUa/L; walnut, less than 0.35 kUa/L; pecan, less than 0.35 kUa/L; peanut, 2.34 kUa/L; almond, 3.7 kUa/L; hazel nut, 16.5 kUa/L. The patient is told to avoid peanut, hazel nut, and almond. However, additional history reveals prior tolerance of peanut, hazel nut, and almonds that were eaten often, even after the cookie reaction incident. However, mild past symptoms from cashew and pistachio had occurred, so typically they were avoided. Cashew and pistachio share similar allergenic proteins. Additional history also reveals that this bakery uses cashew and pistachio in the almond cookies. In addition, the patient has birch pollen and grass pollen allergy, so cross-reactive proteins in these pollens with peanut, hazel nut, and almond

produce positive test results that, in this situation, were not relevant since he already ate these routinely without symptoms. A subsequent serum test shows a pistachio s-IgE level of 1.2 kUa/L. Although the serum test result to cashew was negative, the result of a skin test by an allergist was positive to cashew. Therefore, the patient must avoid cashew and pistachio.

This example teaches several important lessons. First, history is paramount and influences test selection and interpretation. Second, serum s-IgE test has modest sensitivity and specificity and influences include cross-reactivity. Third, caution must be used in test selection, and test panels should be avoided if possible.

*Stinging Insect Allergy*

Often the primary care or emergency department physician is the first to evaluate and treat allergic reactions to stinging insects (eg, honeybee, wasp). These reactions have the potential to be life-threatening, and it is important that these patients receive an appropriate diagnostic evaluation and management plan after treatment of the acute allergic reaction. In general, the allergy specialist should be consulted for patients who have had potentially life-threatening insect stings. A brief summary of diagnosis and management of stinging insect reactions is below. For a more comprehensive review, readers can refer to "Stinging Insect Hypersensitivity: A Practice Parameter Update."[47]

*Allergy Diagnostic Testing Special Considerations: Evaluation of Insect Sting Allergy History*

- Normal (moderate pain, itching, swelling, for a few days)
- Large local (10- to 20-cm swelling for 5–10 days; can be massive)
- Cutaneous systemic (hives, angioedema, flush)
- Anaphylaxis (throat or breathing symptoms, dizziness or hypotension, loss of consciousness, or death)

*Natural History: Chance of a Dangerous Reaction in the Future?*

- Most children "outgrow" cutaneous systemic reactions but not anaphylaxis. The risk of a moderate to severe reaction to a future reaction is less than 5% in children with cutaneous systemic reactions or large local reactions.[48]
- Large local reactions lead to anaphylaxis in less than 5% of cases.
- Risk of anaphylaxis can persist for decades without intervening stings.
- Stinging insect allergic individuals may not always experience anaphylaxis every time they are stung by the insect they are allergic to.

*Diagnostic Tests (Evidence of IgE Antibodies to Venom)*

- Skin tests (more sensitive): preferred method of testing as recommended in the "Stinging Insect Hypersensitivity: A Practice Parameter Update."[47]
- Serum s-IgE (convenient, but false-negative results in 15% of cases)[47]
- Approximately 5% to 10% of patients with negative venom skin test results with a history of a systemic reaction have a positive venom s-IgE test result.[49]

*Quality of Life: Will Fear of Reaction Affect Normal Activities?*

- Counsel on realistic risks of dangerous reactions, use of epinephrine.
- Consider venom immunotherapy.

*Management*

- Referral to allergy specialist for systemic insect sting allergy
  - To make the diagnosis
  - For treatment: venom immunotherapy is indicated for
  - Adults: cutaneous as well as other symptoms of anaphylaxis
  - Children: (16 years and younger): not for cutaneous only

*Summary of the Pearls and Pitfalls of Allergy Diagnostic Testing With Emphasis on the Recommendations in the Allergy Diagnostic Practice Parameters*

Patients often present to the medical practice with the complaints of an "allergic" problem. The medical professional must determine whether this problem is truly allergic (ie, IgE mediated). Allergy is defined as an IgE response with the subsequent release of cellular mediators causing a reaction that may affect the lungs, nose, skin, cardiovascular system, or gastrointestinal tract. A thorough history is the primary tool to determine if the patient's presentation is likely from an allergic cause. Symptoms, seasonal predilection, rapidity of onset, and age of onset all help the clinician search for the diagnosis of allergies. Physical examination findings may further guide the physician. These findings include allergic shiners, nasal crease, boggy nasal turbinates, and pharyngeal cobblestones. Allergy skin test and serum s-IgE can be useful tools in the allergy diagnostic evaluation.

In the diagnosis of suspected IgE-mediated allergic diseases, neither skin tests nor serum s-IgE tests should be either requested or interpreted outside the context of the clinical history and physical examination. Positive test results provide objective confirmation of IgE sensitization, which may support a history of symptoms on exposure to the relevant allergen. In contrast, a negative test result makes allergy to a suspected allergen unlikely. When used indiscriminately, both skin and serum s-IgE tests may commonly be associated with false-positive results and, rarely, false-negative results may occur. Thus, diagnostic tests should be used to support or exclude a diagnosis of specific allergies based on the history. They should almost never be used as a substitute for a careful history or as an allergy screen.

The number of allergens needed to test in a particular area may vary with geographic location and clinical history. Indoor allergens, such as house dust mites, indoor and outdoor fungal allergens, cockroach, cat, and dog, all should be tested for perennial allergic rhinitis. Pollens from trees, grasses, and

weeds are chosen as per the geographic region. Relatively few foods account for most IgE-mediated allergic reactions in both children and adults. In children, these include cow's milk, egg, peanuts, tree nuts, soybeans, and wheat. In adults, these include peanuts, tree nuts, fish, shellfish, clams, fruits, and vegetables. It is important to test for foods that we believe may be the cause of the patient's problems because skin testing for foods is not effective for indiscriminate screening.

The Allergy Diagnostic Practice Parameter states, "The number of skin tests and the allergens selected for skin testing should be determined based on the patient's age, history, environment and living conditions (eg, region of the country), occupation, and activities. Routine use of large numbers of skin tests or routine annual tests without a definite clinical indication are clearly not justified."[1]

*In Vitro: Serum s-IgE Evaluation*

Multiple methods have been used to measure serum allergen s-IgE results. These range from RAST to the method of enzyme/substrate (ImmunoCap, Immulite). The sensitivity of serum s-IgE measurements is generally lower than prick or puncture tests,[2,37–39] but the specificity is greater.[2,3] If the clinical history is positive and the serum s-IgE test result is negative, allergy skin testing should be considered. Serum s-IgE testing is preferred to prick or puncture testing when the patient has severe skin disease, is receiving medications that may suppress skin tests (or cause a reaction or prevent treatment of a reaction) and cannot be removed from them, for uncooperative patients, or if the history suggests a risk of anaphylaxis from the testing.

It is important in serum s-IgE tests, as with skin tests, that results correlate with the history, physical examination findings, and in some cases timing of natural exposure to allergen. Therefore, it is often misleading to choose immunotherapy from remote laboratories based on history alone.

*In Vivo: Skin Testing*

According to the Allergy Diagnostic Practice Parameter, "Prick/puncture tests or intracutaneous tests are the preferred techniques for IgE-mediated hypersensitivity. It is advisable to use prick/puncture devices, which are relatively nontraumatic and elicit reproducible results when placed on specific areas of the body (eg, arms or back). Optimal results depend on use of potent test extracts and proficiency of the skin tester (ie, demonstration of coefficient of variation $\leq$30% at different periods)."[1]

The Allergy Diagnostic Practice Parameter also states, "The reliability of prick/puncture tests depends on the skill of the tester, the test instrument, color of the skin, skin reactivity on the day of the test, potency, and stability of test reagents. For these reasons, sensitivity tends to be higher among pollens, certain foods, dust mite, fungi, and certain epidermals compared with venoms, drugs, and chemicals."[1] The Allergy Diagnostic Practice Parameter states that "although correlation of higher levels of specific-IgE to clinical sensitivity for some allergens is equivalent to prick/puncture tests, skin prick/puncture tests generally have better overall predictability and are the preferred initial diagnostic approach."[1] The use and interpretation of both methods should depend on the clinical history.

In general, allergy diagnostic tests should be used in clinical practice to:

- Assist in confirming or excluding a suspected diagnosis of food allergy
- Assist in confirming or excluding a suspected diagnosis of aeroallergen allergy
- Assist in confirming or excluding the diagnosis of stinging insect hypersensitivity or drug allergy
- Determine the need for environmental control recommendations to reduce exposure to outdoor or indoor aeroallergens
- Demonstrate sensitization to inhalant occupational allergens, which may cause occupational asthma or rhinitis
- Guide selection of aeroallergens for inclusion in allergen immunotherapy extracts

In conclusion, selection of allergy diagnostic tests and interpretation of the results MUST be directed, guided, and viewed in the context of the patient's clinical history.

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